REMARKS

Claims 1-125 are currently pending in the present application. Of these, claims 1-58, 95-123 and 125 have been withdrawn from consideration due to a restriction requirement. Thus claims 59 – 94 and 124 are currently under examination. The Examiner has rejected claims 59-94 and 124 for the reasons set forth below. Reconsideration of the application is respectfully requested in view of the following remarks.

In the Office Action dated February 17, 2004, the Examiner rejected the subject application under 35 U.S.C. §§ 112, first paragraph, 112 second paragraph, 102(b), and 103 and under the judicially-created doctrine of double-patenting.

On pages 2-5 of the Office Action, the Examiner rejected claims 59, 60, 62, 63, 68-94, and 124 under 35 U.S.C. §112, first paragraph, for scope of enablement, and on pages 5-6 of the Office Action, rejected claims 59– 94 and 124 under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Additionally, on pages 6-8 of the Office Action, the Examiner rejected claims 59, 62, 65, 66, 69, and 71 under 35 U.S.C. §102(b), as allegedly anticipated by Connor et al., EP 316630 ("Connor '360") and rejected 59, 62, 65, and 70 under 35 U.S.C. §102(b), as allegedly anticipated by Fujimura et al., Chem. Abstr., vol. 70, no. 3, 20 January 1966, ("Fujimura, CAS 1966") and by Morkhort, Farmakol. Toksikol. (Kiev) 1971, No. 6, pp 108 – 111 ("Morkhort 1971"). On pages 8-11 of the Office Action, the Examiner rejected claims 59, 62, 65, 66, 69, and 77 under 35 U.S.C. §102(b), as allegedly anticipated by Hirano Hiroshi et al., JP 42019583 ("Hiroshi '583"). The Examiner also rejected claims 59 – 94 and 124 under 35 U.S.C. §103, as allegedly unpatentable over Barrett et al., WO 99/01421 ("Barrett '421") in view of Walker et al., British Journal of Pharmacology, Nov. 1993, 36(5), 417 – 25 ("Walker BJP 1993") and Ma et al., Brain Research, Dec 6 1991, 566 (1-2) 95-102 ("Ma BR 1991"). Additionally, on pages 11-13 of the Office Action, the Examiner provisionally rejected claims 59-94 and 124 under the judicially created doctrine of obviousness-type double patenting over claims 1 – 33 of copending Application No. 10/031149 and over all claims of copending Application No. 10/031037. For reasons detailed below, Applicants herein respectfully traverse the rejections.

1. Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 59, 60, 62, 63, 68-94, and 124 under 35 U.S.C. §112, first paragraph, for scope of enablement. The Examiner acknowledged that the specification enables the use of the claimed compounds for "treating particular chronic pain caused by particular diseases/disorders;" however, the Examiner has alleged that the specification does not reasonably provide enablement for "treating any chronic pain caused by any diseases/disorders." Applicants respectfully traverse this rejection.

The Examiner alleged that the specification of the present invention fails to provide information that would enable the skilled artisan to fully practice this invention without undue experimentation. The Examiner cited *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) as indicating that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The Examiner characterized the pharmaceutical art as unpredictable and has asserted that the testing that is disclosed in the specification is insufficient to support the breadth of conditions recited in the claims. Applicants respectfully dispute both the Examiner's characterization of the level of unpredictability of the art and the specificity of the enablement provided by the specification.

Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of non-enablement. Specifically, the Examiner has failed to establish a basis as to why the scope of protection is not adequately enabled by the description of the invention provided in the specification. In order to make a §112, first paragraph rejection the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (An examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure).

The CCPA has stated that it is incumbent upon the Patent Office, whenever a rejection under 35 U.S.C. §112, first paragraph is made, "to explain why it doubts the truth or accuracy of any statement in a supporting disclosure *and to back up assertions of its own with acceptable evidence or reasoning* which is inconsistent with the contested statement. Otherwise, there would be no need for applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971) (emphasis added). Applicants respectfully submit that the Examiner has failed to meet her burdens of explaining why and of backing up assertions with evidence or reasoning. Applicants respectfully submit that the Examiner has provided neither evidence nor reasoning to support her assertion that the claims of the subject application are not enabled.

Applicants note that the Examiner based her rejection on her assertions that "the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity;" and that "the instant invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses any disease states or conditions associated with pain and the symptoms associated with pain, a great numbers [sic] of diseases or disorders such as inflammatory pain, neuropathic pain, and pain caused by migraine, tension headache, cluster headache, and bowel disorder, diopathic [sic] pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hyperthyroidism, which are known to be involved various, many possible, and different, separate and independent etiologies." The Examiner further asserts that "[t]he skilled artisan would view that the treatment of all conditions associated with pain and the symptoms associated pain by administering the particular compound herein is highly unpredictable." (Words and phrases are underlined as in the Examiner's discussion.) In summary, the Examiner has characterized both the pharmaceutical art and the medical art of pain management as being unpredictable. Applicants respectfully dispute both of those characterizations.

In response, applicants initially note respectfully that beyond her own *ipse dixit* the Examiner has provided no actual information or reasoning to support her assertions that the pertinent art of this invention is "unpredictable" and that the claimed invention is "highly unpredictable." Rather, Applicants respectfully submit, the Examiner stated her own personal belief as a premise for the rejection. Applicants submit that the Examiner's unsupported assertions fall far short of the explanation required under *Marzocchi*.

Applicants respectfully submit that while the pharmaceutical art is not an exact science, neither is it characterized by such unpredictability as suggested by the Examiner. Rather, it is widely known in the pharmaceutical art that compounds which are related structurally frequently exhibit similar, though not identical, pharmaceutical properties, and there are many cases of whole families of prominent drugs which share -- and indeed are named for -- structural features, e.g., "tricyclic antidepressants" and "beta-lactam antibiotics." These drugs are used to treat a range of related disorders. Thus, both families of drugs and groups of medical disorders are characterized by broad general trends which, contrary to the Examiner's assertion, impart to the pharmaceutical art in general a moderate level of predictability.

Turning to the particular field of the pharmaceutical treatment of pain, Applicants note that this is not a new field but rather one that has been the subject of active research for many years. Indeed with the understanding that chronic pain differs markedly from non-chronic pain and requires different treatment strategies – an understanding that is summarized at pages 1-2 of the specification

and that is advanced by the teaching of the present invention – the field is becoming ever more predictable. As is well known in the art, chronic pain is characterized by the persistent and repeated firing of pain signals. (See, *e.g.*,www.ninds.nih.gov/health_and_medical/disorders/chronic_pain.htm.) Thus, Applicants respectfully submit that it is not appropriate to characterize the art to which the present invention pertains as one that is "unpredictable."

The Examiner has also characterized the field of pain as very broad and unpredictable, one that ("...encompasses a great numbers of diseases associated or disorders ...which are known to be involved various, many possible, and different, separate and independent etiologies.") In response, Applicants respectfully note that it is well-established that the etiology of chronic pain is common across a variety of disease sources. Furthermore, a major determinant of much chronic pain is neuropathy. Just as inflammation can have many causes but is susceptible to treatment by the same anti-inflammatory agents, the same family of signal-transduction inhibitors is effective in treating chronic pain from many sources. Therefore, Applicants should not be restricted to chronic pain associated with particular disease states/disorders. They are entitled to a claim for the treatment of chronic pain in general.

In addition to disputing the Examiner's characterization of the art as unpredictable, applicants also respectfully dispute the Examiner's evaluation of the degree of enablement provided. The Examiner noted that several compounds of this invention were tested by means of the neuropathic pain model in the rat. Applicants respectfully direct the Examiner's attention to pages 86 – 93 of the specification, wherein are described the currently accepted, standard assays for evaluating treatment of chronic pain. These assays are well-established as being predictive for chronic, and they provide the foundation for the evaluation, development, and regulatory review of drugs for chronic pain: streptozocin-induced static allodynia and chronic constriction injury. Applicants note further that the compounds of the present invention were compared with pregabalin, a compound known to be under development for chronic pain. Thus Applicants disagree with the Examiner's assertion that the instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation.

Applicants further submit that it is not unreasonable for the applicants to claim that the presently described compounds are useful for the treatment of chronic pain, as prior to the filing date of the present application, it was known that Erk activity plays a major role in neuronal response to Ca^{2+} and cAMP signals. See *Neuron* (1999) 23(1):11-14, attached hereto. This publication supports a role for Erk activation in delivering chronic pain signals to the CNS, and thus supports the role of MEK inhibitors in the treatment of chronic pain. This is acknowledged

by the recent review article, Developments in mitogen-induced extracellular kinase 1 inhibitors and their used in the treatment of disease; *Expert Opin. Ther. Patents* (2002) **12** (12), which is also attached hereto. For the examiner's convenience, the Applicants have listed in Appendix A attached hereto, the references that are being provided to the Examiner in support of the Applicants' arguments against the §112, first paragraph rejections.

The Examiner asserts that merely several particular compounds within the claims, i.e., PD 212622, PD 297447, PD 184352, PD 254552 were administered intrathecally to a neuropathic pain model in the rat shown at Example 3 of the specification. She concludes from this that the evidence in the examples is not commensurate in scope with the claimed invention and does not demonstrate criticality of a wide spectrum of disease states associated pain in the claimed method and a claimed range of the compounds. The Examiner has cited MPEP §716.02(d). Applicants respectfully submit that the Examiner has misconstrued the application of the law from this particular section of MPEP. MPEP §716.02(d) relates to unexpected results commensurate in scope with a claimed invention and is thus concerned with obviousness issues, not issues of enablement. Applicants fail to see what this section has to do with enablement. In contrast to the Examiner's characterization of the data, the *Expert Opinion* reference referred to in the preceding paragraph refers (on page 1806, 2nd column) to WO application of the present application and the fact that the MEK inhibitor PD184352 delivered through intrathecal injection was found to temporarily block pain as efficiently as pregabalin **in support of the fact that MEK1/2 inhibitors show promise in the treatment of arthritis and chronic pain** (see section 4.2.2 of the above mentioned *Expert Opinion* reference). Applicants respectfully submit that they have amply demonstrated the general utility of MEK inhibitors in the treatment of chronic pain.

Thus, in summary, Applicants respectfully submit that the Examiner has not succeeded in making out a *prima facie* case of non- enablement in the present application. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, first paragraph.

2. Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 59– 94 and 124 under 35 U.S.C. §112, second paragraph. The Examiner has alleged that these claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Specifically, the Examiner alleged that the claim term "a subject" is not clearly defined in the claims or in the specification and that the use of "a subject" therefore renders these claims indefinite. The Examiner asserts that one of ordinary skill in the art could interpret that the term "subject" would be a single cell, any biological system, an animal or a human, and thus one of ordinary skill in the art could not interpret the metes and bounds of the patent protection desired as to what "a subject" encompassed thereby. Applicants respectfully traverse the rejection on the ground that one skilled in the art is well aware of the meaning of this term, and thus the recitation of "a subject" in the claims is not indefinite.

The phrase "a subject" as used in the present application in its plain and ordinary sense as understood by those of ordinary skill in the art, and refers to both human and non-human subjects, such as animals. When not defined by applicant in the specification, the words of a claim must be given their plain meaning. In other words, they must be read as they would be interpreted by those of ordinary skill in the art. *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1342, 60 USPQ2d 1851, 1854 (Fed. Cir. 2001). "[W]ords in patent claims are given their ordinary meaning in the usage of the field of the invention, unless the text of the patent makes clear that a word was used with a special meaning." *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299, 53 USPQ2d 1065, 1067 (Fed. Cir. 1999).

Applicants contend the plain and ordinary meaning of "subject" is clear to those of ordinary skill in the art. Applicants have conducted a search of the U.S. patent literature from 2001 to the present, and have come up with a list of 265 issued U.S. patents where the term "subject" is used along with the words "treat" and "method" in the claims. Applicants have found that the vast majority of these issued patents have method of treatment claims wherein the word "subject" is used in claim language. Furthermore a large number of these U.S. patents do not have a definition of the term "subject". This supports Applicants' contention, that the term is well understood by those of ordinary skill in the art. No specific definition of "subject" required in the specification. Accordingly, applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

3. Rejections under 35 U.S.C. §102(b)

The Examiner rejected claims 59, 62, 65, 66, 69, and 71 under 35 U.S.C. §102(b), as allegedly anticipated by Connor et al. (EP 0316630A, Warner Lambert Co.) The Examiner alleges that Connor et al. discloses that the active compounds of formula I which read on the instant compounds (Examiner refers to Examples 13 and 18 of Connor et. al.), being cyclooxygenase inhibitors, are useful in pharmaceutical compositions and methods for treating inflammation, arthritis, and pain (referring to abstract, page 4, lines 35-37, pages 7-8, and claims 1-17). Applicants respectfully traverse the rejection. Applicants note that Connor et al. refers to the compounds in question as being useful in treating inflammation, arthritis, and pain, whereas, by contrast, claims 59, 62, 65, 66, 69, and 71 teach a method for treating *chronic pain* using the recited compounds. As chronic pain is different from ordinary or acute pain, as discussed further hereinbelow, claims 59, 62, 65, 66, 69, and 71 are not anticipated by Connor et al. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner rejected claims 59, 62, 65, and 70 under 35 U.S.C. §102(b), as allegedly anticipated by Fujimura, H et al.: "HYDROXAMIC ACID DERIVATIVES", Chemical Abstracts & Indexes, ACS, Columbus, US, Vol. 70, No.3, 20 January 1966 (1969-01-20), or JP 42 024578 A or JP 42019583 B4 (Takeda Chemical Industrial Ltd.). The Examiner alleged that Fujimura *CAS* 1966 discloses that the active compounds of formula I which read on compounds of the present invention are active as analgesics. Applicants respectfully traverse the rejection. Applicants note that Fujimura *CAS* 1966 refers to the compounds in question as analgesics, whereas, by contrast, claims 59, 62, 65, and 70 are directed to a method for treating *chronic pain* using the recited compounds. As chronic pain is different from ordinary or acute pain, as discussed further hereinbelow, claims 59, 62, 65, and 70 are not anticipated by Fujimara *CAS* 1966. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner rejected claims 59, 62, 65, and 69 under 35 U.S.C. §102(b), as allegedly anticipated by Morkhort 1971 (Abstract of Farmakol. Toksikol. (Kiev), (1971), No. 6, 108-11). The Examiner alleged that Morkhort 1971 discloses that the active compounds therein which read on compounds of the present invention are active as analgesics. Applicants respectfully traverse the rejection. Applicants note that Morkhort 1971discloses that the compounds in question are analgesics, whereas, by contrast, claims 59, 62, 65, and 69 are directed toward a method for treating chronic pain using the recited compounds. As chronic pain is different from ordinary or acute pain, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner rejected claims 59, 62, 65, 69, and 77 under 35 U.S.C. §102(b), as allegedly anticipated by Hirano Hiroshi et al. (JP 42019583 B4, Takeda Chemical Industrial Ltd., 1967). The Examiner alleged that Hirano Hiroshi discloses that the active compounds of formula I which read on compounds of the present invention are active as analgesics. Applicants respectfully traverse the rejection. Applicants note that Hirano Hiroshi et al. discloses that the compounds in question are analgesics, whereas, by contrast, claims 59, 62, 65, 69, and 77 are directed to a method for treating chronic pain using the recited compounds. As chronic pain is different from ordinary or acute pain, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

In each of the anticipation rejection above, the Examiner asserts that as the purported use of the compounds in question is as an analgesic, therefore, these references anticipate the presently claimed use of the recited compounds in the treatment of chronic pain. Applicants wish to stress herein that chronic pain is different from ordinary pain. As set forth in the attached NINDS Chronic Pain Information Page (www.ninds.nih.gov):

> "While acute pain is a normal sensation triggered in the nervous system to alert you to possible injury and the need to take care of yourself, chronic pain is different. Chronic pain persists. Pain signals keep firing in the nervous system for weeks, months, even years. There may have been an initial mishap -- sprained back, serious infection, or there may be an ongoing cause of pain -- arthritis, cancer, ear infection, but some people suffer chronic pain in the absence of any past injury or evidence of body damage. Many chronic pain conditions affect older adults. Common chronic pain complaints include headache, low back pain, cancer pain, arthritis pain, neurogenic pain (pain resulting from damage to the peripheral nerves or to the central nervous system itself), psychogenic pain (pain not due to past disease or injury or any visible sign of damage inside or outside the nervous system)."

Thus chronic pain is distinct from ordinary or acute pain, and an analgesic used for ordinary or acute pain does not necessarily have utility or efficacy in the treatment of chronic pain. The Examiner has not set forth any reason why the purported use of the recited compounds in the references cited also make them useful in the treatment of chronic pain.

To anticipate a claim, a reference must teach each and every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil*

Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). None of the presently cited references teach that the active compounds recited therein are useful in the treatment of chronic pain. Since the element of chronic pain is not taught by the references, they cannot anticipate the presently rejected claims. Applicants therefore respectfully request the Examiner to withdraw the present anticipation rejection.

4. Rejection under 35 U.S.C. §103

The Examiner rejected claims 59 – 94 and 124 under 35 U.S.C. §103, as allegedly unpatentable over Barrett (WO 99/01421) in view of Walker (British Journal of Clinical Pharmacology, (1993 Nov.) 36 (5) 417-25) and Ma (Brain Research, (1991 Dec 6) 566 (1-2) 95-102).

The Examiner cited Barrett for allegedly disclosing that the active compounds of formula I which read on the instant compounds, have covered the instant compounds, or are structurally substantially similar to the instant compounds (referring to formula II, II and IIIa at pages 5-6, and e.g., Example 212), being MEK inhibitors, are useful in pharmaceutical compositions and methods for treating inflammation (referring to abstract, pages 1-3, and claims 1-34 of Barrett). The Examiner acknowledges that Barrett does not expressly disclose the employment of the particular MEK inhibitors therein, in methods of treating chronic pain. The Examiner cites Ma for allegedly teaching that pain (e.g., neuropathic pain) is known to be associated with MEK (referring to "abstract" in particular). The Examiner cites Walker for allegedly teaching that pain is well-known to be associated with inflammation (referring to "abstract" in particular).

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular MEK inhibitors of Barrett in methods of treating chronic pain. The Examiner's reasoning is as follows: One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular MEK inhibitors of Barrett in methods of treating chronic pain, because particular MEK inhibitors of Barrett is known to be useful in methods of inflammation according to Barrett. It is also known that pain (e.g., neuropathic pain) is known to be associated with MEK according to Ma. Moreover, pain is well-known to be associated with inflammation according to Walker. The Examiner further asserts that some of the instant compounds read on the compounds of Barrett, while other compounds are structurally substantially similar. The Examiner cites MPEP 2144 for the proposition that if the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species. Applicants respectfully disagree with the position taken by the Examiner

and traverse this rejection. Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness in the present rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142.

None of the three references cited alone or in combination teach anything about the treatment of chronic pain as presently claimed. It is respectfully submitted that the Examiner has misconstrued the teaching of Ma. The Examiner characterized Ma as allegedly teaching that pain is known to be associated with MEK. However, the "MEK" referred to in Ma is not the same as the "MEK" referred to in the present application. "MEK" in Ma refers to Met-enkephalin, and has nothing to do with "MEK inhibitors" of the present invention. In the present invention, "MEK" refers to "mitogen-induced extracellular kinase". Met-enkephalin has no relationship at all with inhibitors of mitogen-induced extracellular kinase. Furthermore, while Ma may refer to pain, there is no reference at all to *chronic* pain. It is respectfully pointed out that neurophathic pain is nowhere disclosed in Ma and furthermore that naturopathic pain is a subset of chronic pain. On page 1, lines 8-9 of the present specification, it is clearly set forth that chronic pain includes neuropathic pain, and chronic inflammatory pain. The Examiner's reference to neuropathic pain as being an example of "pain" disclosed in Ma is therefore misleading and in error. The Examiner has therefore misconstrued the teaching of Ma, owing to any lack of reference in Ma to "mitogen-induced extracellular kinase" inhibitors and to chronic pain. Therefore, there is no motivation for a person of ordinary skill in the art to employ the MEK inhibitors of Barrett in the treatment of chronic pain. None of the three references, Barrett, Walker or Ma provides the motivation to utilize the compounds disclosed in Barrett for treating chronic pain.

Applicants also respectfully direct the Examiner's attention to the specification, at page 2, lines 6-7, wherein it is taught that the efficacy of anti-inflammatory agents toward chronic pain is weak. Therefore, even if the anti-inflammatory agents of Barrett were utilized for the treatment of chronic pain, there would be no reasonable expectation of success.

Applicants respectfully submit that since all three references are silent as to treatment of chronic pain, no combination of those references would make the present invention obvious. Applicants therefore request the Examiner to withdraw the present rejection.

5. Obviousness-type Double Patenting Rejection

The Examiner provisionally rejected claims 59-64 and 124 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-33 of copending Application No. 10/031149. The Examiner asserts that although the conflicting claims are not identical, thy are not patentably distinct from each other because the copending application is drawn to the same method of treatment, chronic pain, as the instant claimed method, employing the same or structurally substantially similar to the instant compounds. The Examiner asserts that there is substantial overlap between the instant claims and the claims of the copending application. Applicants disagree with the Examiner and traverse this rejection.

A double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). MPEP 804.

Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are employed when making an obvious-type double patenting analysis. These factual inquiries are summarized as follows:

(A) Determine the scope and content of a patent claim and the prior art relative to a claim in the application at issue;

(B) Determine the differences between the scope and content of the patent claim and the prior art as determined in (A) and the claim in the application at issue;

(C) Determine the level of ordinary skill in the pertinent art; and

(D) Evaluate any objective indicia of nonobviousness.

The conclusion of obviousness-type double patenting is made in light of these factual determinations. Any obviousness-type double patenting rejection should make clear:

(A) The differences between the inventions defined by the conflicting claims - a claim in the patent compared to a claim in the application; and

(B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent.

In the present case, the Examiner has failed to establish a *prima facie* case of obviousness between the claims of the '149 application and the present claims, as set forth below.

Comparison of the claims 1-33 of copending Application No. 10/311149 with the presently rejected claims of the instant invention reveal that not only claims not identical, they are substantially different. The Examiner's attention is directed to the fact that in the presently claimed chemical compounds of formula I(B), the top substituent on the left phenyl ring is -C(O)W where W is as defined in the present application. On the other hand, the top substituent in the left phenyl ring of the compounds of formula (I) of the '149 application is W wherein here W is a heterocyclic moiety as shown by formula (i) – (xiii) in claim 1 of the '149 application. There is no carbonyl (-C=O) group attached to the top carbon atom of the left phenyl ring as there is in the presently claimed compounds. The top carbon atom of the left phenyl ring of the presently claimed compounds is not directly attached to a heterocyclic moiety as required by the claimed of the '149 application.

Furthermore the "J" substituent of the presently claimed compounds is not iodine as is required by the compounds of formula (I) of the '149 application. Thus there are substantial differences in chemical structure between the compounds of formula (I)B as presently claimed the compounds of formula (I) as set forth in the claims of the '149 application. There is no overlap between the rejected claims of the present application and claims 1-33 of the '149 application. The Examiner has not provided any reason why one of ordinary skill in the art, having knowledge of the compounds of formula (I) of the '149 application would be motivated to prepare the presently claimed compounds of formula (I)(B) when the chemical structures are so substantially different. Therefore, Applicants respectfully request the Examiner to withdraw this rejection.

The Examiner has also provisionally rejected claims 59-64 and 124 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over all claims of copending Application No. 10/031037. The Examiner asserts that although the conflicting claims are not identical, thy are not patentably distinct from each other because the copending application is drawn to the same method of treatment, chronic pain, as the instant claimed method, employing the same or structurally substantially similar to the instant

compounds. The Examiner asserts that there is substantial overlap between the instant claims and the claims of the copending application. Applicants again disagree with the Examiner on the ground that the Examiner has failed to establish a prima facie case of obviousness between the present claims and those of the copending application, and traverse this rejection.

Again, comparison of the claims of copending Application No. 10/031037 with the presently rejected claims of the instant invention reveal that not only claims not identical, they are substantially different. Most notably, the Examiner's attention is directed to the fact that the left phenyl ring of formula I in the claims of the '037 application has a bromine or iodine group in a position meta to the $-N(R_2)-$ group. In contrast, the analogous right phenyl ring of formula (I)B of the presently claimed compounds has a "J" substituent that cannot be a bromine or iodine. The "J" substituents set forth in the presently claimed invention are vastly different from a halogen. Thus there are substantial differences in chemical structure between the compounds of formula (I)B as presently claimed the compounds of formula I as set forth in the claims of the '037 application. There is no overlap between the rejected claims of the present application and the claims of the '037 application. The Examiner has not provided any reason why one of ordinary skill in the art, having knowledge of the compounds of formula I of the '037 application would be motivated to prepare the presently claimed compounds of formula (I)B when the chemical structures are so substantially different. Therefore, Applicants respectfully request the Examiner to withdraw this rejection.

CONCLUSION

Applicants respectfully request prompt reconsideration of claims 59-94 and 124 and early allowance of the application.

If the Examiner wishes to comment or discuss any aspect of this application or response, applicants' undersigned attorney invites the Examiner to call him at the telephone number provided below.

Respectfully submitted,

Date: August 16, 2004

Krishna G. Banerjee

Krishna G. Banerjee
Attorney for Applicant(s)
Reg. No. 43,317

Pfizer, Inc
Patent Department, 5th Floor
150 East 42nd Street
New York, NY 10017-5612
(212) 733-5310

Appendix A

(List of references being provided to Examiner)

1. www.ninds.nih.gov/health_and_medical/disorders/chronic_pain.htm.;

2. *Neuron* (1999) 23(1):11-14;

3. *Expert Opin. Ther. Patents* (2002) **12** (12).